EXHIBIT B

Vivus withdraws NDA for Alibra

Vivus has withdrawn the US marketing application for its second-generation transurethral treatment for male erectile dysfunction, Alibra (alprostadil plus prazosin). Company shares ended at $3 on October 20th, on the news, but dropped by 14.6% to $2.56 when trading resumed on the following Monday.

The company would not give the reason for the withdrawal but said it plans to meet the US FDA soon to determine whet additional information is needed to obtain approval for the product. Following this and a meeting with the EMEA to discuss the EC application, Vivus will decide on its future plans for Alibra, company CEO Leland Wilson says.

Vivus filed for US approval of Alibra in December last year after the product was found to be more effective in treating erectile dysfunction than its first-generation product, MUSE (transurethral alprostadil), with the added benefit of a single-strength dosage formulation. The company also filed for EC approval of Alibra in June (*Scrip* No 2548, p 17).

Recent sales of MUSE, which is widely available, have also slowed, the company reported. The product is continuing to suffer from competition with Pfizer's Viagra (sildenafil). Vivus had US gross product revenue of $5 million for the third quarter compared with $5.6 million for the same period of 1999. Vivus says the decline is due to lower product use by veterans administration hospitals as a result of Viagra being added to the permitted drug list earlier this year. The company reported a third-quarter net income of $208,000 compared with $897,000 during the same period of 1999.

Gliatech withdraws PMA for Adcon-L

Gliatech has withdrawn its supplementary pre-market application (PMA) for its lead product, Adcon-L – a gel to prevent post-surgical scarring – following discussions with the US FDA about an earlier external investigation which found that good clinical practice was not maintained in a US post-approval study. The company's share price dropped six cents to $5.50 on the news, barely up from the year low of $5.25.

Adcon-L was approved in the US in May 1998 based on positive results from a pivotal European trial and interim data from a US study. But in August this year, the FDA raised concerns about updated results from the US trial, and issued a Form 483 report questioning the recording of data and its presentation to the agency (*Scrip* No 2572, p 9).

The FDA's concerns were a big blow to the company. Its share price dropped 60% in September and Guilford Pharmaceuticals called off the proposed merger between the companies. A class action lawsuit was filed over the matter, which also led to Gliatech's president and CEO Dr Thomas Oesterling, and other executives, resigning (*Scrip* No 2579, p 6).

In response, Gliatech has proposed re-evaluating the MRI data from the trial under controlled conditions using an independent, blinded evaluator. It is also hiring consultants to review its clinical studies and training management process, and has added more managers and staff members to its clinical research and quality assurance department.

The company's problems with Adcon-L do not affect its continued marketing, it notes. Gliatech also believes that the clinical and patient experiences with Adcon-L – in more than 165,000 procedures – show the safety and efficacy of the product. However, the company does not know yet whether further studies will be needed, it told *Scrip*.

Lilly pulls out of R-fluoxetine deal

Lilly has pulled out of a licensing deal with Sepracor for the development of (R)-fluoxetine, a single-isomer version of Lilly's SSRI antidepressant, Prozac (fluoxetine), following concerns over QTc prolongation with the product.

Sepracor has also stopped development of the product. The company had been expecting royalties of between $50 and $100 million by 2003 from Lilly for the product, and the setback caused its shares to decline by 28%, closing at $87 on the day of the news.

This is a further blow for Lilly's Prozac franchise. The company licensed the rights to (R)-fluoxetine in 1998, and had hoped to transfer Prozac patients to the product before the arrival of generic competition. However, this strategy looked unlikely to succeed when, in August, a US court rejected Lilly's method-of-use patent for Prozac, thus stripping the product of nearly three years' protection. The ruling paved the way for generic products to reach the market as early as February next year, and led to a 31% fall in Lilly's share price, even though Lilly continued to claim that the single isomer could carve out its own niche as a stand-alone product (*Scrip* Nos 2566, p 7 & 2567, p 8).

A review of all available clinical data for (R)-fluoxetine, involving 2,000 patients, showed that, at the highest dose tested, the isomer demonstrated a small but statistically significant increase in QTc prolongation. Sepracor said this was "probably clinically irrelevant or insignificant". It is unclear whether QTc prolongation leads to human morbidity or mortality. The targeted dose of the isomer in clinical trials was eight times the amount of (R)-fluoxetine contained in Prozac, Sepracor said, although it added that the development of a lower dose was not being considered because safety trials would delay a US submission by at least another two years.

But Dr Gary Tollefson, head of Lilly's neuroscience product group, told analysts that Prozac circulating in the body contained only about 20-25% of the R-enantiomer, and that the company's starting point was to quadruple the dose. He agreed that evidence of a dose-dependent increase in QTc prolongation was clearly a safety problem, but he also conceded that the product did not meet the necessary efficacy criteria.

The changing marketplace for antidepressants may also have played a role in Lilly's decision to terminate the programme, Sepracor's CEO Tim Barberich says. Clinicians are moving beyond SSRI agents, and are looking to agents with multiple actions. Lilly has duloxetine, a serotonin and noradrenaline re-uptake inhibitor, in late-stage development and Sepracor's (R)-DDMS is in Phase II. (R)-DDMS combines the benefits of an SSRI with those of a noradrenaline and dopamine re-uptake inhibitor, and "is the most potent of these compounds that we know of", Sepracor claims.

Sepracor has 10 products in the clinic, and plans to launch some of them itself, it says. In addition, the company licensed the metabolite of the top-selling antihistamine, loratadine (Claritin), desloratadine, to Schering-Plough, for which US approval is expected later this year. The product was recently recommended for approval in the EC.

Sepracor's pipeline includes the novel antihistamine, norastemizole, which is in Phase III trials with an NDA filing due in January 2001; (S)-zopiclone in Phase III trials as a hypnotic; (S)-oxybutynin, which is scheduled to begin Phase III trials for urge incontinence in the first quarter of 2001; and (R,R)-formoterol, which should enter Phase III trials in early 2001 as the first beta-agonist for the treatment of asthma and emphysema.